

# WEST Search History

DATE: Thursday, April 25, 2002

<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
side by side			result set
<i>DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR</i>			
L11	(B-factor adj value) or (nmr adj order adj parameter) or (amide adj protection adj factor)	2	L11
L10	L9 same (epitope\$4 or antigen\$4 )	816	L10
L9	L8 same admini\$8	2054	L9
L8	L5 same immun\$8	20230	L8
L7	L6 and admini\$8	42272	L7
L6	L5 and immun\$8	89657	L6
L5	s (B-factor adj value) or (nmr adj order adj parameter) or (amide adj protection adj factor)	4844473	L5
L4	altered adj peptide adj ligand\$4	27	L4
L3	L2 and immun\$8	16	L3
L2	L1 and protein	25	L2
L1	(landry)[IN]	1093	L1

END OF SEARCH HISTORY

=> dis his

(FILE 'HOME' ENTERED AT 10:56:02 ON 25 APR 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 10:56:11 ON 25 APR 2002  
L1 10596 S (ALTERED) (1N) (PEPTIDE? OR PROTEIN?)  
L2 0 S L1 AND ( B-FACTOR OR (NMR (1N) ORDER (1N) PARAMETER) OR (AMID  
L3 1157 S (PEPTIDE OR PROTEIN OR ANTIGEN OR EPITOPE) AND ( B-FACTOR OR  
L4 11 S L3 AND ADMINIST?  
L5 8 DUP REM L4 (3 DUPLICATES REMOVED)  
L6 25604 S (PEPTIDE? OR PROTEIN? OR ANTIGEN? OR EPITOPE?) AND ( (B (1N)  
L7 0 S L6 AND ADMINIST?  
L8 992 S L6 AND ADMINIST?  
L9 361 S L8 AND (ENHANCE? OR STIMULAT? IR INCREAS? OR AUGMENT?)  
L10 197 S L9 AND PD<20000420  
L11 168 DUP REM L10 (29 DUPLICATES REMOVED)  
L12 147 S (PEPTIDE? OR PROTEIN? OR ANTIGEN? OR EPITOPE?) AND ( (B (1N)  
L13 0 S L12 AND ADMINIST?  
L14 289 S ( (B (1N) FACTOR (1N) VALUE) OR (NMR (1N) ORDER (1N) PARAMET  
L15 17 S L14 AND IMMUN?  
L16 7 DUP REM L15 (10 DUPLICATES REMOVED)  
L17 1157 S (PEPTIDE OR PROTEIN OR ANTIGEN OR EPITOPE) AND ( B-FACTOR OR  
L18 502 S LANDRY S?/AU  
L19 137 S L18 AND PROTEIN  
L20 21 S L19 AND IMMUN?

=> end

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	321.16	321.37
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-14.25	-14.25

STN INTERNATIONAL LOGOFF AT 11:37:37 ON 25 APR 2002

=> dis his

(FILE 'HOME' ENTERED AT 10:56:02 ON 25 APR 2002)

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L8 992 S L6 AND ADMINIST?  
L9 361 S L8 AND (ENHANCE? OR STIMULAT? IR INCREAS? OR AUGMENT?)  
L10 197 S L9 AND PD<20000420  
L11 168 DUP REM L10 (29 DUPLICATES REMOVED)  
L12 147 S (PEPTIDE? OR PROTEIN? OR ANTIGEN? OR EPITOPE?) AND ( (B (1N)

=> s l12 and administ?  
L13 0 L12 AND ADMINIST?

=> s ( (B (1N) factor (1N) value) or (nmr (1N) order (1N) parameter?) or (amide (1N) protection (1N) factor?) )  
L14 289 ((B (1N) FACTOR (1N) VALUE) OR (NMR (1N) ORDER (1N) PARAMETER?)  
OR (AMIDE (1N) PROTECTION (1N) FACTOR?) )

=> s l14 and immun?  
L15 17 L14 AND IMMUN?

=> dup rem 115  
PROCESSING COMPLETED FOR L15  
L16 7 DUP REM L15 (10 DUPLICATES REMOVED)

=> dis l16 ibib abs

L16 ANSWER 1 OF 7 MEDLINE DUPLICATE 1  
ACCESSION NUMBER: 2001514895 MEDLINE  
DOCUMENT NUMBER: 21446879 PubMed ID: 11562944  
TITLE: Protein molecular dynamics with the generalized Born/ACE  
solvent model.  
AUTHOR: Calmet N; Schaefer M; Simonson T  
CORPORATE SOURCE: Laboratoire de Biologie et Genomique Structurales (CNRS),  
Institut de Génétique et Biologie Moléculaire et  
Cellulaire, Strasbourg-Illkirch, France.  
SOURCE: PROTEINS, (2001 Nov 1) 45 (2) 144-58.  
PUB. COUNTRY: Journal code: PTS; 8700181. ISSN: 0887-3585.  
LANGUAGE: United States  
FILE SEGMENT: English  
ENTRY MONTH: Priority Journals  
ENTRY DATE: 200111  
Entered STN: 20010920  
Last Updated on STN: 20011105  
Entered Medline: 20011101

AB Implicit solvent models are increasingly important for the study of  
proteins in aqueous solution. Here, the generalized Born (GB) solvent  
polarization model as implemented in the analytical ACE potential  
[Schaefer and Karplus (1996) J Phys Chem 100:1578] is used to perform  
molecular dynamics simulations of two small, homologous proteins: the  
immunoglobulin-binding domain of streptococcal protein G and the  
Ras binding domain of Raf. Several model parameterizations are compared  
through more than 60 ns of simulation. Results are compared with two  
simpler solvent models—an accessible surface area model and a  
distant-dependent dielectric model, with finite-difference Poisson  
calculations, with existing explicit solvent simulations, and with  
experimental data. The simpler models yield stable but distorted  
structures. The best GB/ACE implementation uses a set of atomic Voronoi  
volumes reported recently, obtained by averaging over a large database of  
crystallographic protein structures. A 20% reduction is applied to the  
volumes, compensating in an average sense for an excessive de-screening of  
individual charges inherent in the ACE self-energy and for an  
undersolvation of dipolar groups inherent in the GB screening function.  
This GB/ACE parameterization yields stable trajectories on the 0.5-1-ns  
time scale that deviate moderately (approximately 1.5-2.5 Å) from the  
X-ray structure, reproduce approximately the surface distribution of  
charged, polar, and hydrophobic groups, and reproduce accurately backbone  
flexibility as measured by amide NMR-order  
parameters. Over longer time scales (1.5-3 ns), some of the  
protein G runs escape from the native energy basin and deviate strongly (3  
Å) from the native structure. The conformations sampled during the  
transition out of the native energy basin are overstabilized by the GB/ACE  
solvation model, as compared with a numerical treatment of the full  
dielectric continuum model.  
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=> dis l16 ibib abs 1-7

L16 ANSWER 1 OF 7 MEDLINE DUPLICATE 1  
ACCESSION NUMBER: 2001514895 MEDLINE  
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AUTHOR: Calmet N; Schaefer M; Simonson T  
CORPORATE SOURCE: Laboratoire de Biologie et Genomique Structurales (CNRS),  
Institut de Génétique et Biologie Moléculaire et  
Cellulaire, Strasbourg-Illkirch, France.  
SOURCE: PROTEINS, (2001 Nov 1) 45 (2) 144-58.  
PUB. COUNTRY: Journal code: PTS; 8700181. ISSN: 0887-3585.  
LANGUAGE: United States  
FILE SEGMENT: English  
ENTRY MONTH: Priority Journals  
ENTRY DATE: 200111  
Entered STN: 20010920  
Last Updated on STN: 20011105  
Entered Medline: 20011101

AB Implicit solvent models are increasingly important for the study of  
proteins in aqueous solution. Here, the generalized Born (GB) solvent  
polarization model as implemented in the analytical ACE potential  
[Schaefer and Karplus (1996) J Phys Chem 100:1578] is used to perform  
molecular dynamics simulations of two small, homologous proteins: the

immunoglobulin-binding domain of streptococcal protein G and the Ras binding domain of Raf. Several model parameterizations are compared through more than 60 ns of simulation. Results are compared with two simpler solvent models—an accessible surface area model and a distant-dependent dielectric model, with finite-difference Poisson calculations, with existing explicit solvent simulations, and with experimental data. The simpler models yield stable but distorted structures. The best GB/ACE implementation uses a set of atomic Voronoi volumes reported recently, obtained by averaging over a large database of crystallographic protein structures. A 20% reduction is applied to the volumes, compensating in an average sense for an excessive de-screening of individual charges inherent in the ACE self-energy and for an undersolvation of dipolar groups inherent in the GB screening function. This GB/ACE parameterization yields stable trajectories on the 0.5-1-ns time scale that deviate moderately (approximately 1.5-2.5 Å) from the X-ray structure, reproduce approximately the surface distribution of charged, polar, and hydrophobic groups, and reproduce accurately backbone flexibility as measured by amide NMR-order parameters. Over longer time scales (1.5-3 ns), some of the protein G runs escape from the native energy basin and deviate strongly (3 Å) from the native structure. The conformations sampled during the transition out of the native energy basin are overstabilized by the GB/ACE solvation model, as compared with a numerical treatment of the full dielectric continuum model.

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L16 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 19991113565 CAPLUS  
 DOCUMENT NUMBER: 1301181469  
 TITLE: Prediction, detection, and design of T cell epitopes  
 INVENTOR(S): Landry, Samuel J.  
 PATENT ASSIGNEE(S): The Administrators of the Tulane Educational Fund, USA  
 SOURCE: PCT Int. Appl., 95 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906061	A1	19990211	WO 1998-US15563	19980728
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: CH, GM, KE, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9885952	A1	19990222	AU 1998-85952	19980728
PRIORITY APPLN. INFO.:			US 1997-54156P	P 19970729
			WO 1998-US15563	W 19980728

AB The invention features a method which allows detection and creation of immunodominant T cell epitopes in an antigen. This method allows the generation of improved vaccines with which to prevent and/or treat diseases. In addn., detection of T lymphocytes which react to immunodominant T cell epitopes is facilitated by the method of the invention. Manipulation of the epitopes detected using this method allows the generation of tolerogens which can inhibit the immune response to the antigen. The identified T cell epitopes from allergen, pathogen or neoplastic cell are useful for treating allergy, autoimmune disease and as vaccine for cancer therapy. Thus, T cell epitopes of Hsp10 protein, Staphylococcal nuclease, hen egg lysozyme, cytochrome c, and HIV gp120, and T cell epitope in bacteriophage T4 Gp31 were depicted.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 7 MEDLINE DUPLICATE 2  
 ACCESSION NUMBER: 95163250 MEDLINE  
 DOCUMENT NUMBER: 95163250 PubMed ID: 7859418  
 TITLE: The value of complement activation products in the assessment of systemic lupus erythematosus flares.  
 AUTHOR: Porcel J M; Ordi J; Castro-Salomo A; Vilardell M; Rodrigo M J; Gene T; Warburton F; Kraus M; Vergani D  
 CORPORATE SOURCE: Department of Immunology, King's College Hospital, London, United Kingdom.  
 SOURCE: CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY, (1995 Mar) 74 (3) 283-8.  
 PUB. COUNTRY: United States  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199503  
 ENTRY DATE: Entered STN: 19950404  
 Last Updated on STN: 19950404  
 Entered Medline: 19950323

AB Complement activation products (CAP) have been reported as sensitive markers of disease activity in systemic lupus erythematosus (SLE). We have measured seven parameters of the complement system (C3, C4, factor B, C3a, C4a, iC3b, and the terminal complement complex-TCC-) in 61 SLE patients to study their interrelationship and relative efficacy as diagnostic indicators of lupus activity. Disease activity was judged according to a clinical index (SLEDAI) to be active in 22 and inactive in 39 patients. Subjects with active SLE showed increased levels of C3a, C4a, and TCC compared with those of stable lupus and normal controls, and plasma concentrations of these CAP manifested a positive correlation with disease activity scores. However, values of factor B and iC3b did not correlate with lupus flares. Serum C3 levels were a better reflection of the degree of SLE activity than were C4 levels. The anaphylatoxins were extremely sensitive markers of disease activity but they lacked enough specificity, and iC3b was not at all informative for this purpose. On the whole, TCC concentration was the most useful parameter (77% sensitivity, 80% specificity) to monitor lupus activity, correlating the best with the activity scoring system, and thus offers a better laboratory marker of lupus severity than conventional measurements of complement.

L16 ANSWER 4 OF 7 MEDLINE DUPLICATE 3  
 ACCESSION NUMBER: 93058245 MEDLINE  
 DOCUMENT NUMBER: 93058245 PubMed ID: 1432491

TITLE: Activation of human complement system in paracoccidioidomycosis.  
 COMMENT: Erratum in: J Med Vet Mycol 1992;30(6):489  
 AUTHOR: Munk M E; Kajdacsy-Balla A; Del Negro G; Cuce L C; Da Silva W D  
 CORPORATE SOURCE: Departamento de Imunologia, Universidade de Sao Paulo, Brazil.  
 SOURCE: JOURNAL OF MEDICAL AND VETERINARY MYCOLOGY, (1992) 30 (4) 317-21.  
 JOURNAL code: JMD; 8605493. ISSN: 0268-1218.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199212  
 ENTRY DATE: Entered STN: 19930122  
 Last Updated on STN: 19990129  
 Entered Medline: 19921218

AB Plasma samples of 14 patients with paracoccidioidomycosis were analysed for components that represent activation of the complement system. Most patients (12/13) showed significant titres of complement-fixing antibodies and 14/14 had increased C4d/C4 ratios. There was no conclusive correlation between these two immunological indices, however. Factor B values of patients were similar to normal donors and fragment Ba was not detected in any of the patients. These results indicate a classical complement pathway activation in the plasma of patients with paracoccidioidomycosis.

L16 ANSWER 5 OF 7 MEDLINE  
 ACCESSION NUMBER: 92234253 MEDLINE  
 DOCUMENT NUMBER: 92234253 PubMed ID: 1568647  
 TITLE: Activation of the classical complement pathway in spontaneous bacterial peritonitis.  
 AUTHOR: Bird G; Senaldi G; Panos M; Rolando N; Alexander G; Vergani D; Williams R  
 CORPORATE SOURCE: Institute of Liver Studies, King's College, School of Medicine and Dentistry, London.  
 SOURCE: GUT, (1992 Mar) 33 (3) 307-11.  
 JOURNAL code: FVT; 2985108R. ISSN: 0017-5749.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
 ENTRY MONTH: 199205  
 ENTRY DATE: Entered STN: 19920612  
 Last Updated on STN: 19990129  
 Entered Medline: 19920528

AB To investigate the possibility that low complement concentrations in the plasma and ascites of patients with severe liver disease could be secondary to complement consumption, complement activation was studied in 32 patients with severe liver disease, 11 of whom had spontaneous bacterial peritonitis (SBP). In patients with SBP, plasma C3 and C4 were significantly lower than in uninfected patients (mean values 0.74 v 1.13 g/l, p less than 0.01 and 0.20 v 0.28 g/l, p less than 0.05 respectively). Plasma complement activation via the classical pathway, as shown by C4d/C4, was significantly increased in patients with SBP compared with uninfected patients (37.3 v 22.2, p less than 0.01) as was C3d/C3 (14.0 v 8.11, p less than 0.01), but there was no significant difference in Ba/B between SBP and uninfected patients. Ascitic C3 concentrations were higher in patients without SBP than in infected patients (0.37 v 0.08 g/l, p less than 0.05), as were factor B values (0.11 v 0.03 g/l, p less than 0.05). There was no significant difference in ascitic C4 concentrations in patients with SBP compared with uninfected patients (0.03 v 0.07 g/l). Although consumption of C3, as shown by C3d/C3 in ascites, was increased in infected patients compared with uninfected patients (79.1 v 36.1, p less than 0.05), there was no difference in ascitic complement activation between the groups for either the classical or alternative pathways. In SBP, decreased plasma C3 and C4 are primarily caused by increased activation of the classical pathway and not impaired hepatic synthesis. Activation and consumption of C3 is one factor causing the low ascitic C3 concentrations observed in SBP.

L16 ANSWER 6 OF 7 MEDLINE DUPLICATE 4  
 ACCESSION NUMBER: 86258715 MEDLINE  
 DOCUMENT NUMBER: 86258715 PubMed ID: 3088536  
 TITLE: The alternative pathway of complement in sheep during the course of infection with *Trypanosoma congoense* and after Berenil treatment.  
 AUTHOR: Malu M N; Tabel H  
 SOURCE: PARASITE IMMUNOLOGY, (1986 May) 8 (3) 217-29.  
 JOURNAL code: OQU; 7910948. ISSN: 0141-9838.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 198607  
 ENTRY DATE: Entered STN: 19900321  
 Last Updated on STN: 19990129  
 Entered Medline: 19860725

AB Experimental *T. congoense* infections in sheep resulted in a striking decrease in parameters of the alternative complement pathway (ACP), ie. factor B, C3 and haemolytic complement activity (HA) initiated via the ACP. The levels of factor B, C3 and HA declined before, during and after the first wave of parasitemia which reached a peak at day 8. Levels of 20 to 25% of normal values (factor B) and 20% (C3, HA) persisted throughout the course of the infection. After Berenil treatment, when no parasites were detected in blood, their serum levels remained low. They returned to normal values about 8 (factor B) to 20 days (C3, HA) after trypanocidal treatment. Serum concentrations of factor B were significantly elevated in some, but not all sheep 6 days after infection with *T. congoense*. The sheep were tested for their potential state of immuno-modulation by immunization with *Brucella abortus* 4 days after trypanocidal treatment. In contrast to other sheep, the sheep which had shown early elevated serum factor B levels were found to express immune enhancement. It is suggested that there might be a positive correlation between the degree of enhanced serum levels of factor B at the early stage of infection and enhanced immune responsiveness.

L16 ANSWER 7 OF 7 MEDLINE  
 ACCESSION NUMBER: 77030318 MEDLINE  
 DOCUMENT NUMBER: 77030318 PubMed ID: 1068203

TITLE: Activation of the alternative pathway of complement in childhood acute lymphoblastic leukemia.  
AUTHOR: Kalwinsky D K; Urnsom J R; Stitzel A E; Spitzer R E  
SOURCE: JOURNAL OF LABORATORY AND CLINICAL MEDICINE, (1976 Nov) 88 (5) 745-56.  
Journal code: IVR; 0375375. ISSN: 0022-2143.  
PUB. COUNTRY: United States  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 197612  
ENTRY DATE: Entered STN: 19900313  
Last Updated on STN: 19900313  
Entered Medline: 19761230

AB Sequential studies in children with acute lymphoblastic leukemia have demonstrated that at diagnosis or relapse there is defective utilization of complement by the alternative pathway. Thus, the sera of 17/18 patients fail to completely consume C3 to C9 when incubated with zymosan or cobra venom factor (CoF). This underutilization is due to a specific inhibitor of C3 activation which has been partially isolated. By remission, the inhibitor disappears and the CoF and zymosan assays return to normal. In addition, serum levels of C3 and factor B are elevated at the time of diagnosis or relapse but fall to below 3 S.D. from the mean in nearly 60 per cent of the cases during induction therapy. Similarly, serum C4 levels which are normal at diagnosis fall to less than 3 S.D. from the mean in 7/12 cases during treatment. Low C3 levels correlate well with factor B values, suggesting that if C3 to C9 are utilized after the inhibitor has been eliminated, such utilization occurs primarily through the alternative pathway. Presumably, as illustrated by the low C4 levels, this activity is mediated by the amplification loop of the alternative pathway involving classical pathway generation of C3b.

=> s (peptide or protein or antigen or epitope) and ( B-factor or (nmr (1N) order (1N) parameter) or (amide (1N) protection (1N) factor) )  
2 FILES SEARCHED...  
L17 1157 (PEPTIDE OR PROTEIN OR ANTIGEN OR EPITOPE) AND (B-FACTOR OR (NMR (1N) ORDER (1N) PARAMETER) OR (AMIDE (1N) PROTECTION (1N) FACTOR) )

=> dis his

(FILE 'HOME' ENTERED AT 10:56:02 ON 25 APR 2002)

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L1 10596 S (ALTERED) (1N) (PEPTIDE? OR PROTEIN?)  
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L6 25604 S (PEPTIDE? OR PROTEIN? OR ANTIGEN? OR EPITOPE?) AND ( (B (1N)  
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L9 361 S L8 AND (ENHANCE? OR STIMULAT? IR INCREAS? OR AUGMENT?)  
L10 197 S L9 AND PD<20000420  
L11 168 DUP REM L10 (29 DUPLICATES REMOVED)  
L12 147 S (PEPTIDE? OR PROTEIN? OR ANTIGEN? OR EPITOPE?) AND ( (B (1N)  
L13 0 S L12 AND ADMINIST?  
L14 289 S ( (B (1N) FACTOR (1N) VALUE) OR (NMR (1N) ORDER (1N) PARAMET  
L15 17 S L14 AND IMMUN?  
L16 7 DUP REM L15 (10 DUPLICATES REMOVED)  
L17 1157 S (PEPTIDE OR PROTEIN OR ANTIGEN OR EPITOPE) AND ( B-FACTOR OR

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=> s landry S?/au  
L18 502 LANDRY S?/AU

=> s l18 and protein  
L19 137 L18 AND PROTEIN

=> s l19 and immun?  
3 FILES SEARCHED...  
L20 21 L19 AND IMMUN?

=> dis l20 1-21 ibib abs

L20 ANSWER 1 OF 21 MEDLINE  
ACCESSION NUMBER: 2002050948 MEDLINE  
DOCUMENT NUMBER: 21634825 PubMed ID: 11602571  
TITLE: Structural basis for helper T-cell and antibody epitope immunodominance in bacteriophage T4 Hsp10. Role of disordered loops.  
AUTHOR: Dai Guixiang; Carmicle Stephanie; Steede N Kalaya;  
Landry Samuel J  
CORPORATE SOURCE: Department of Biochemistry, Tulane University Health Sciences Center, New Orleans, Louisiana 70112-2699, USA.  
CONTRACT NUMBER: R01-AI42350 (NIAID)  
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Jan 4) 277 (1)  
161-8.  
Journal code: 2985121R. ISSN: 0021-9258.  
PUB. COUNTRY: United States  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200201  
ENTRY DATE: Entered STN: 20020125  
Last Updated on STN: 20020128  
Entered Medline: 20020124

AB Antigen three-dimensional structure potentially limits the access of endoproteolytic processing enzymes to cleavage sites and of class II major histocompatibility antigen-presenting proteins to helper T-cell epitopes. Helper T-cell epitopes in bacteriophage T4 Hsp10 have been mapped by restimulation of splenocytes from CBA/J and C57BL/6J mice immunized in conjunction with mutant (R192G) heat-labile enterotoxin from *Escherichia coli*. Promiscuously immunogenic sequences were associated with unstable loops in the three-dimensional structure of T4 Hsp10. The immunodominant sequence lies on the N-terminal flank of the 22-residue mobile loop, which is sensitive to proteolysis in divergent Hsp10s. Several mobile loop deletions that inhibited proteolysis in vitro caused global changes in the helper T-cell

epitope map. A mobile loop deletion that strongly stabilized the protein dramatically reduced the immunogenicity of the flanking immunodominant helper T-cell epitope, although the protein retained good overall immunogenicity. Antisera against the mobile loop deletion variants exhibited increased cross-reactivity, most especially the antisera against the strongly stabilized variant. The results support the hypothesis that unstable loops promote the presentation of flanking epitopes and suggest that loop deletion could be a general strategy to increase the breadth and strength of an immune response.

L20 ANSWER 2 OF 21 MEDLINE  
ACCESSION NUMBER: 2002050947 MEDLINE  
DOCUMENT NUMBER: 21634843 PubMed ID: 11673463  
TITLE: Proteolytic sensitivity and helper T-cell epitope immunodominance associated with the mobile loop in Hsp10s.  
AUTHOR: Carmicle Stephanie; Dai Guixiang; Steede N Kalaya; Landry Samuel J  
CORPORATE SOURCE: Department of Biochemistry, Tulane University Health Sciences Center, New Orleans, Louisiana 70112-2699, USA.  
CONTRACT NUMBER: R01-AI42350 (NIAID)  
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Jan 4) 277 (1) 155-60.  
Journal code: 2985121R. ISSN: 0021-9258.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200201  
ENTRY DATE: Entered STN: 20020125  
Last Updated on STN: 20020128  
Entered Medline: 20020124

AB Antigen three-dimensional structure potentially limits antigen processing and presentation to helper T-cell epitopes. The association of helper T-cell epitopes with the mobile loop in Hsp10s from mycobacteria and bacteriophage T4 suggests that the mobile loop facilitates proteolytic processing and presentation of adjacent sequences. Sites of initial proteolytic cleavage were mapped in divergent Hsp10s after treatment with a variety of proteases including cathepsin S. Each protease preferentially cleaved the Hsp10s in the mobile loop. Flexibility in the 22-residue mobile loop most probably allows it to conform to protease active sites. Three variants of the bacteriophage T4 Hsp10 were constructed with deletions in the mobile loop to test the hypothesis that shorter loops would be less sensitive to proteolysis. The two largest deletions effectively inhibited proteolysis by several proteases. Circular dichroism spectra and chemical cross-linking of the deletion variants indicate that the secondary and quaternary structures of the variants are native-like, and all three variants were more thermostable than the wild-type Hsp10. Local structural flexibility appears to be a general requirement for proteolytic sensitivity, and thus, it could be an important factor in antigen processing and helper T-cell epitope immunogenicity.

L20 ANSWER 3 OF 21 MEDLINE  
ACCESSION NUMBER: 2001641671 MEDLINE  
DOCUMENT NUMBER: 21551246 PubMed ID: 11551929  
TITLE: Allocation of helper T-cell epitope immunodominance according to three-dimensional structure in the human immunodeficiency virus type I envelope glycoprotein gp120.  
AUTHOR: Dai G; Steede N K; Landry S J  
CORPORATE SOURCE: Department of Biochemistry, Tulane University Health Sciences Center, New Orleans, Louisiana 70112, USA.  
CONTRACT NUMBER: R21-AI42702 (NIAID)  
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Nov 9) 276 (45) 41913-20.  
Journal code: 2985121R. ISSN: 0021-9258.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200112  
ENTRY DATE: Entered STN: 20011107  
Last Updated on STN: 20020123  
Entered Medline: 20011205

AB The specificity and intensity of CD4(+) helper T-cell responses determine the effectiveness of immune effector functions. Promiscuously immunodominant helper T-cell epitopes in the human immunodeficiency virus (HIV) envelope glycoprotein gp120 could be important in the development of broadly protective immunity, but the underlying mechanisms of immunodominance and promiscuity remain poorly defined. In this study, gp120 helper T-cell epitopes were systematically mapped in CBA/J and BALB/c mice by restimulation assays using a set of overlapping peptides spanning the entire sequence of the gp120 encoded by HIV strain 89.6. The results were analyzed in the context of the HIV gp120 structure determined by x-ray crystallography. One major finding was that all of the promiscuously immunodominant gp120 sequences are located in the outer domain. Further analyses indicated that epitope immunogenicity in the outer domain correlates with structural disorder in adjacent N-terminal segments, as indicated by crystallographic B-factors or sequence divergence. In contrast, the correlation was poor when the analysis encompassed the entire gp120 sequence or was restricted to only the inner domain. These findings suggest that local disorder promotes the processing and presentation of adjacent epitopes in the outer domain of gp120 and therefore reveal how three-dimensional structure shapes the profile of helper T-cell epitope immunogenicity.

L20 ANSWER 4 OF 21 MEDLINE  
ACCESSION NUMBER: 2001323360 MEDLINE  
DOCUMENT NUMBER: 21135678 PubMed ID: 11238401  
TITLE: The gits5 Gbeta and git11 Ggamma form an atypical Gbetagamma dimer acting in the fission yeast glucose/cAMP pathway.  
AUTHOR: Landry S; Hoffman C S  
CORPORATE SOURCE: Department of Biology, Boston College, Chestnut Hill, Massachusetts 02467, USA.  
CONTRACT NUMBER: GM-46226 (NIGMS)  
SOURCE: GENETICS, (2001 Mar) 157 (3) 1159-68.  
Journal code: FNH; 0374636. ISSN: 0016-6731.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English

FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200106  
 ENTRY DATE: Entered STN: 20010611  
 Last Updated on STN: 20010611  
 Entered Medline: 20010607

AB Fission yeast adenylate cyclase, like mammalian adenylate cyclases, is regulated by a heterotrimeric G protein. The gpa2 Galpha and git5 Gbeta are both required for glucose-triggered cAMP signaling. The git5 Gbeta is a unique member of the Gbeta family in that it lacks an amino-terminal coiled-coil domain shown to be essential for mammalian Gbeta folding and interaction with Ggamma subunits. Using a git5 bait in a two-hybrid screen, we identified the git11 Ggamma gene. Co-immunoprecipitation studies confirm the composition of this Gbetagamma dimer. Cells deleted for git11 are defective in glucose repression of both fbp1 transcription and sexual development, resembling cells lacking either the gpa2 Galpha or the git5 Gbeta. Overexpression of the gpa2 Galpha partially suppresses loss of either the git5 Gbeta or the git11 Ggamma, while mutational activation of the Galpha fully suppresses loss of either Gbeta or Ggamma. Deletion of gpa2 (Galpha), git5 (Gbeta), or git11 (Ggamma) confer quantitatively distinct effects on fbp1 repression, indicating that the gpa2 Galpha subunit remains partially active in the absence of the Gbetagamma dimer and that the git5 Gbeta subunit remains partially active in the absence of the git11 Ggamma subunit. The addition of the CAAK box from the git11 Ggamma to the carboxy-terminus of the git5 Gbeta partially suppresses the loss of the Ggamma. Thus the Ggamma in this system is presumably required for localization of the Gbetagamma dimer but not for folding of the Gbeta subunit. In mammalian cells, the essential roles of the Gbeta amino-terminal coiled-coil domains and Ggamma partners in Gbeta folding may therefore reflect a mechanism used by cells that express multiple forms of both Gbeta and Ggamma subunits to regulate the composition and activity of its G proteins.

L20 ANSWER 5 OF 21 MEDLINE  
 ACCESSION NUMBER: 2000183814 MEDLINE  
 DOCUMENT NUMBER: 20183814 PubMed ID: 10716904  
 TITLE: Helper T-cell epitope immunodominance associated with structurally stable segments of hen egg lysozyme and HIV gp120.  
 AUTHOR: Landry S J  
 CORPORATE SOURCE: Department of Biochemistry, Tulane University School of Medicine, 1430 Tulane Avenue, New Orleans, LA 70112, USA.. landry@mailhost.tcs.tulane.edu  
 CONTRACT NUMBER: R01AI42350 (NIAID)  
 R21AI42702 (NIAID)  
 SOURCE: JOURNAL OF THEORETICAL BIOLOGY, (2000 Apr 7) 203 (3) 189-201.  
 PUB. COUNTRY: Journal code: K8N; 0376342. ISSN: 0022-5193.  
 ENGLAND: United Kingdom  
 LANGUAGE: Journal; Article; (JOURNAL ARTICLE)  
 FILE SEGMENT: English  
 ENTRY MONTH: 200004  
 ENTRY DATE: Entered STN: 20000505  
 Last Updated on STN: 20000505  
 Entered Medline: 20000426

AB Although many antigen sequences potentially can bind to the MHCII proteins, only a small number of epitopes dominate the immune response. Additional mechanisms of processing, presentation or recognition must restrict the immune response against a large portion of the antigen. A highly significant correlation is found between epitope immunodominance and local structural stability in hen egg lysozyme. Since antigen proteins are likely to retain substantial native-like structure in the processing compartment, protease action may be focused on regions that are most readily accommodated in the protease active sites, and thus, the intervening sequence are preferentially presented. Immunodominance also correlates with sequence conservation as expected from the constraints imposed by structure. These results suggest that the three-dimensional structure of the antigen limits the immune response against some antigen segments. For HIV gp120, a substantial improvement in the accuracy of epitope prediction is obtained by combining rules for MHCII binding with a restriction of the predicted epitopes to well-conserved sequences.  
 Copyright 2000 Academic Press.

L20 ANSWER 6 OF 21 MEDLINE  
 ACCESSION NUMBER: 1998047507 MEDLINE  
 DOCUMENT NUMBER: 98047507 PubMed ID: 9386348  
 TITLE: Local protein instability predictive of helper T-cell epitopes.  
 AUTHOR: Landry S J  
 CORPORATE SOURCE: Dept of Biochemistry, Tulane University School of Medicine, New Orleans, LA 70112, USA.. landry@mailhost.tcs.tulane.edu  
 SOURCE: IMMUNOLOGY TODAY, (1997 Nov) 18 (11) 527-32. Ref: 32  
 Journal code: AEA; 8008346. ISSN: 0167-5699.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 LANGUAGE: Journal; Article; (JOURNAL ARTICLE)  
 FILE SEGMENT: General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 ENTRY MONTH: English  
 ENTRY DATE: 199801  
 Entered STN: 19980206  
 Last Updated on STN: 19980206  
 Entered Medline: 19980126

AB Although selectivity at the levels of peptide binding to major histocompatibility complex (MHC) class II and recognition by T cells may partially account for immunodominance patterns, it is clear that differential antigen processing also exerts a strong effect. Here, Sam Landry correlates immunodominant epitopes with nearby structurally unstable segments, as identified by hydrogen-deuterium exchange nuclear magnetic resonance (NMR), and suggests that epitope presentation is directed by preferential proteolytic cleavage at the unstable sites.

L20 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:37493 CAPLUS  
 DOCUMENT NUMBER: 136:215109  
 TITLE: Structural basis for helper T-cell and antibody epitope immunodominance in bacteriophage T4 Hsp10. Role of disordered loops

AUTHOR(S): Dai, Guixiang; Carmicle, Stephanie; Steede, N. Kalaya; Landry, Samuel J.

CORPORATE SOURCE: Department of Biochemistry, Tulane University Health Sciences Center, New Orleans, LA, 70112-2699, USA

SOURCE: Journal of Biological Chemistry (2002), 277(1), 161-168

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Antigen three-dimensional structure potentially limits the access of endoproteolytic processing enzymes to cleavage sites and of class II major histocompatibility antigen-presenting proteins to helper T-cell epitopes. Helper T-cell epitopes in bacteriophage T4 Hsp10 have been mapped by restimulation of splenocytes from CBA/J and C57BL/6J mice immunized in conjunction with mutant (R192G) heat-labile enterotoxin from *Escherichia coli*. Promiscuously immunogenic sequences were associated with unstable loops in the three-dimensional structure of T4 Hsp10. The immunodominant sequence lies on the N-terminal flank of the 22-residue mobile loop, which is sensitive to proteolysis in divergent Hsp10s. Several mobile loop deletions that inhibited proteolysis in vitro caused global changes in the helper T-cell epitope map. A mobile loop deletion that strongly stabilized the protein dramatically reduced the immunogenicity of the flanking immunodominant helper T-cell epitope, although the protein retained good overall immunogenicity. Antisera against the mobile loop deletion variants exhibited increased cross-reactivity, most esp. the antisera against the strongly stabilized variant. The results support the hypothesis that unstable loops promote the presentation of flanking epitopes and suggest that loop deletion could be a general strategy to increase the breadth and strength of an immune response.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:37492 CAPLUS

DOCUMENT NUMBER: 136:215108

TITLE: Proteolytic sensitivity and helper T-cell epitope immunodominance associated with the mobile loop in Hsp10s

AUTHOR(S): Carmicle, Stephanie; Dai, Guixiang; Steede, N. Kalaya; Landry, Samuel J.

CORPORATE SOURCE: Department of Biochemistry, Tulane University Health Sciences Center, New Orleans, LA, 70112-2699, USA

SOURCE: Journal of Biological Chemistry (2002), 277(1), 155-160

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Antigen three-dimensional structure potentially limits antigen processing and presentation to helper T-cell epitopes. The assocn. of helper T-cell epitopes with the mobile loop in Hsp10s from mycobacteria and bacteriophage T4 suggests that the mobile loop facilitates proteolytic processing and presentation of adjacent sequences. Sites of initial proteolytic cleavage were mapped in divergent Hsp10s after treatment with a variety of proteases including cathepsin S. Each protease preferentially cleaved the Hsp10s in the mobile loop. Flexibility in the 22-residue mobile loop most probably allows it to conform to protease active sites. Three variants of the bacteriophage T4 Hsp10 were constructed with deletions in the mobile loop to test the hypothesis that shorter loops would be less sensitive to proteolysis. The two largest deletions effectively inhibited proteolysis by several proteases. CD spectra and chem. crosslinking of the deletion variants indicate that the secondary and quaternary structures of the variants are native-like, and all three variants were more thermostable than the wild-type Hsp10. Local structural flexibility appears to be a general requirement for proteolytic sensitivity, and thus, it could be an important factor in antigen processing and helper T-cell epitope immunogenicity.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:845463 CAPLUS

DOCUMENT NUMBER: 136:117255

TITLE: Allocation of helper T-cell epitope immunodominance according to three-dimensional structure in the human immunodeficiency virus type I envelope glycoprotein gp120

AUTHOR(S): Dai, Guixiang; Steede, N. Kalaya; Landry, Samuel J.

CORPORATE SOURCE: Department of Biochemistry, Tulane University Health Sciences Center, New Orleans, LA, 70112, USA

SOURCE: Journal of Biological Chemistry (2001), 276(45), 41913-41920

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The specificity and intensity of CD4+ helper T-cell responses determine the effectiveness of immune effector functions. Promiscuously immunodominant helper T-cell epitopes in the human immunodeficiency virus (HIV) envelope glycoprotein gp120 could be important in the development of broadly protective immunity, but the underlying mechanisms of immunodominance and promiscuity remain poorly defined. In this study, gp120 helper T-cell epitopes were systematically mapped in CBA/J and BALB/c mice by restimulation assays using a set of overlapping peptides spanning the entire sequence of the gp120 encoded by HIV strain 89.6. The results were analyzed in the context of the HIV gp120 structure determined by x-ray crystallography. One major finding was that all of the promiscuously immunodominant gp120 sequences are located in the outer domain. Further analyses indicated that epitope immunogenicity in the outer domain correlates with structural disorder in adjacent N-terminal segments, as indicated by crystallographic B-factors or sequence divergence. In contrast, the correlation was poor when the analysis encompassed the entire gp120 sequence or was restricted to only the inner domain. These findings suggest that local disorder promotes the processing and presentation of adjacent

epitopes in the outer domain of gp120 and therefore reveal how three-dimensional structure shapes the profile of helper T-cell epitope immunogenicity.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:258759 CAPLUS  
DOCUMENT NUMBER: 136:32427  
TITLE: The git5 G.beta. and git11 G.gamma. form an atypical G.beta..gamma. dimer acting in the fission yeast glucose/cAMP pathway  
AUTHOR(S): Landry, Sheila; Hoffman, Charles S.  
CORPORATE SOURCE: Department of Biology, Boston College, Chestnut Hill, MA, 02467, USA  
SOURCE: Genetics (2001), 157(3), 1159-1168  
CODEN: GENTAE; ISSN: 0016-6731  
PUBLISHER: Genetics Society of America  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Fission yeast adenylyl cyclase, like mammalian adenylyl cyclases, is regulated by a heterotrimeric G protein. The gpa2 G.alpha. and git5 G.beta. are both required for glucose-triggered cAMP signaling. The git5 G.beta. is a unique member of the G.beta. family in that it lacks an amino-terminal coiled-coil domain shown to be essential for mammalian G.beta. folding and interaction with G.gamma. subunits. Using a git5 bait in a two-hybrid screen, we identified the git11 G.gamma. gene. Co-immunoprecipitation studies confirm the compn. of this G.beta..gamma. dimer. Cells deleted for git11 are defective in glucose repression of both fbp1 transcription and sexual development, resembling cells lacking either the gpa2 G.alpha. or the git5 G.beta.. Overexpression of the gpa2 G.alpha. partially suppresses loss of either the git5 G.beta. or the git11 G.gamma., while mutational activation of the G.alpha. fully suppresses loss of either G.beta. or G.gamma.. Deletion of gpa2 (G.alpha.), git5 (G.beta.), or git11 (G.gamma.) confer quant. distinct effects on fbp1 repression, indicating that the gpa2 G.alpha. subunit remains partially active in the absence of the G.beta..gamma. dimer and that the git5 G.beta. subunit remains partially active in the absence of the git11 G.gamma. subunit. The addn. of the CAA box from the git11 G.gamma. to the carboxy-terminus of the git5 G.beta. partially suppresses the loss of the G.gamma.. Thus the G.gamma. in this system is presumably required for localization of the G.beta..gamma. dimer but not for folding of the G.beta. subunit. In mammalian cells, the essential roles of the G.beta. amino-terminal coiled-coil domains and G.gamma. partners in G.beta. folding may therefore reflect a mechanism used by cells that express multiple forms of both G.beta. and G.gamma. subunits to regulate the compn. and activity of its G proteins.  
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:169229 CAPLUS  
DOCUMENT NUMBER: 133:295027  
TITLE: Helper T-cell Epitope Immunodominance  
Associated with Structurally Stable Segments of Hen Egg Lysozyme and HIV gp120  
AUTHOR(S): Landry, Samuel J.  
CORPORATE SOURCE: Department of Biochemistry, Tulane University School of Medicine, New Orleans, LA, 70112, USA  
SOURCE: Journal of Theoretical Biology (2000), 203(3), 189-201  
CODEN: JTBIAP; ISSN: 0022-5193  
PUBLISHER: Academic Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Although many antigen sequences potentially can bind to the MHC class II (MHCII) proteins, only a small no. of epitopes dominate the immune response. Addnl. mechanisms of processing, presentation, or recognition must restrict the immune response against a large portion of the antigen. A highly significant correlation is found between epitope immunodominance and local structural stability in hen egg lysozyme. Since antigen proteins are likely to retain substantial native-like structure in the processing compartment, protease action may be focused on regions that are most readily accommodated in the protease active sites, and thus, the intervening sequence are preferentially presented. Immunodominance also correlates with sequence conservation as expected from the constraints imposed by structure. These results suggest that the 3-dimensional structure of the antigen limits the immune response against some antigen segments. For HIV gp120, a substantial improvement in the accuracy of epitope prediction is obtained by combining rules for MHCII binding with a restriction of the predicted epitopes to well-conserved sequences. (c) 2000 Academic Press.  
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:1113565 CAPLUS  
DOCUMENT NUMBER: 130:181469  
TITLE: Prediction, detection, and design of T cell epitopes  
INVENTOR(S): Landry, Samuel J.  
PATENT ASSIGNEE(S): The Administrators of the Tulane Educational Fund, USA  
SOURCE: PCT Int. Appl., 95 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906061	A1	19990211	WO 1998-US15563	19980728
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW, GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9885952	A1	19990222	AU 1998-85952	19980728
PRIORITY APPLN. INFO.:			US 1997-54156P	P 19970729
			WO 1998-US15563	W 19980728

AB The invention features a method which allows detection and creation of immunodominant T cell epitopes in an antigen. This method allows the generation of improved vaccines with which to prevent and/or treat diseases. In addn., detection of T lymphocytes which react to immunodominant T cell epitopes is facilitated by the method of the invention. Manipulation of the epitopes detected using this method allows the generation of tolerogens which can inhibit the immune response to the antigen. The identified T cell epitopes from allergen, pathogen or neoplastic cell are useful for treating allergy, autoimmune disease and as vaccine for cancer therapy. Thus, T cell epitopes of Hep10 protein, Staphylococcal nuclease, hen egg lysozyme, cytochrome c, and HIV gp120, and T cell epitope in bacteriophage T4 Gp31 were depicted.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1997:742032 CAPLUS  
DOCUMENT NUMBER: 128:33419  
TITLE: Local protein instability predictive of helper T-cell epitopes  
AUTHOR(S): Landry, Samuel J.  
CORPORATE SOURCE: Dept. of Biochem., Tulane Univ. Sch. of Med., New Orleans, LA, 70112, USA  
SOURCE: Immunol. Today (1997), 18(11), 527-532  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English  
AB A review with 32 refs. discussing immunodominant helper T-cell epitopes near highly flexible loops, structural instability mapped by crystallog. B-factors, and structural instability mapped by hydrogen-deuterium exchange NMR.

L20 ANSWER 14 OF 21 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 2001107800 EMBASE  
TITLE: The git5 G.beta. and git11 G.gamma. form an atypical G.beta..gamma. dimer acting in the fission yeast glucose/cAMP pathway.  
AUTHOR: Landry S.; Hoffman C.S.  
CORPORATE SOURCE: C.S. Hoffman, Boston College, Biology Department, Higgins Hall 401B, Chestnut Hill, MA 02467, United States.  
hofmacs@bc.edu  
SOURCE: Genetics, (2001) 157/3 (1159-1168).  
Refs: 45  
ISSN: 0016-6731 CODEN: GENTAE  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 004 Microbiology  
021 Developmental Biology and Teratology  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Fission yeast adenylate cyclase, like mammalian adenylate cyclases, is regulated by a heterotrimeric G protein. The gpa2 G.alpha. and git5 G.beta. are both required for glucose-triggered cAMP signaling. The git5 G.beta. is a unique member of the G.beta. family in that it lacks an amino-terminal coiled-coil domain shown to be essential for mammalian G.beta. folding and interaction with G.gamma. subunits. Using a git5 bait in a two-hybrid screen, we identified the git11 G.gamma. gene. Co-immunoprecipitation studies confirm the composition of this G.beta. dimer. Cells deleted for git11 are defective in glucose repression of both fbp1 transcription and sexual development, resembling cells lacking either the gpa2 G.alpha. or the git5 G.beta.. Overexpression of the gpa2 G.alpha. partially suppresses loss of either the git5 G.beta. or the git11 G.gamma., while mutational activation of the G.alpha. fully suppresses loss of either G.beta. or G.gamma.. Deletion of gpa2 (G.alpha.), git5 (G.beta.), or git11 (G.gamma.) confer quantitatively distinct effects on fbp1 repression, indicating that the gpa2 G.alpha. subunit remains partially active in the absence of the G.beta. dimer and that the git5 G.beta. subunit remains partially active in the absence of the git11 G.gamma. subunit. The addition of the CAAAX box from the git11 G.gamma. to the carboxy-terminus of the git5 G.beta. partially suppresses the loss of the G.gamma.. Thus the G.gamma. in this system is presumably required for localization of the G.beta. dimer but not for folding of the G.beta. subunit. In mammalian cells, the essential roles of the G.beta. amino-terminal coiled-coil domains and G.gamma. partners in G.beta. folding may therefore reflect a mechanism used by cells that express multiple forms of both G.beta. and G.gamma. subunits to regulate the composition and activity of its G proteins.

L20 ANSWER 15 OF 21 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 2000311263 EMBASE  
TITLE: Helper T-cell epitope immunodominance associated with structurally stable segments of hen egg lysozyme and HIV gp120.  
AUTHOR: Landry S.J.  
CORPORATE SOURCE: S.J. Landry, Department of Biochemistry, Tulane University School of Medicine, 1430 Tulane Avenue, New Orleans, LA 70112, United States. landry@mailhost.tcs.tulane.edu  
SOURCE: Journal of Theoretical Biology, (7 Apr 2000) 203/3 (189-201).  
Refs: 63  
ISSN: 0022-5193 CODEN: JTBIAP  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 026 Immunology, Serology and Transplantation  
029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Although many antigen sequences potentially can bind to the MHCII proteins, only a small number of epitopes dominate the immune response. Additional mechanisms of processing, presentation or recognition must restrict the immune response against a large portion of the antigen. A highly significant correlation is found between epitope immunodominance and local structural stability in hen egg lysozyme. Since antigen proteins are likely to retain substantial native-like structure in the processing compartment, protease action may be focused on regions that are most readily accommodated in the protease active sites, and thus, the intervening sequence are preferentially presented. Immunodominance also correlates with sequence conservation as expected from the constraints imposed by structure. These results suggest that the three-dimensional structure of the antigen limits the immune response against some antigen

segments. For HIV gp120, a substantial improvement in the accuracy of epitope prediction is obtained by combining rules for MHCII binding with a restriction of the predicted epitopes to well-conserved sequences. (C) 2000 Academic Press.

L20 ANSWER 16 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:118581 BIOSIS  
DOCUMENT NUMBER: PREV200200118581  
TITLE: Structural basis for helper T-cell and antibody epitope immunodominance in bacteriophage T4 Hsp10. Role of disordered loops.  
AUTHOR(S): Dai, Guixiang; Carmicle, Stephanie; Steede, N. Kalaya; Landry, Samuel J. (1)  
CORPORATE SOURCE: (1) Dept. of Biochemistry, Tulane University Health Sciences Center, 1430 Tulane Ave., New Orleans, LA, 70112-2699; landry@tulane.edu USA  
SOURCE: Journal of Biological Chemistry, (January 4, 2002) Vol. 277, No. 1, pp. 161-168. <http://www.jbc.org/>. print.  
ISSN: 0021-9258.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
AB Antigen three-dimensional structure potentially limits the access of endoproteolytic processing enzymes to cleavage sites and of class II major histocompatibility antigen-presenting proteins to helper T-cell epitopes. Helper T-cell epitopes in bacteriophage T4 Hsp10 have been mapped by restimulation of splenocytes from CBA/J and C57BL/6J mice immunized in conjunction with mutant (R192G) heat-labile enterotoxin from Escherichia coli. Promiscuously immunogenic sequences were associated with unstable loops in the three-dimensional structure of T4 Hsp10. The immunodominant sequence lies on the N-terminal flank of the 22-residue mobile loop, which is sensitive to proteolysis in divergent Hsp10s. Several mobile loop deletions that inhibited proteolysis in vitro caused global changes in the helper T-cell epitope map. A mobile loop deletion that strongly stabilized the protein dramatically reduced the immunogenicity of the flanking immunodominant helper T-cell epitope, although the protein retained good overall immunogenicity. Antisera against the mobile loop deletion variants exhibited increased cross-reactivity, most especially the antisera against the strongly stabilized variant. The results support the hypothesis that unstable loops promote the presentation of flanking epitopes and suggest that loop deletion could be a general strategy to increase the breadth and strength of an immune response.

L20 ANSWER 17 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:118580 BIOSIS  
DOCUMENT NUMBER: PREV200200118580  
TITLE: Proteolytic sensitivity and helper T-cell epitope immunodominance associated with the mobile loop in Hsp10s.  
AUTHOR(S): Carmicle, Stephanie; Dai, Guixiang; Steede, N. Kalaya; Landry, Samuel J. (1)  
CORPORATE SOURCE: (1) Dept. of Biochemistry, Tulane University Health Sciences Center, 1430 Tulane Ave., New Orleans, LA, 70112-2699; landry@tulane.edu USA  
SOURCE: Journal of Biological Chemistry, (January 4, 2002) Vol. 277, No. 1, pp. 155-160. <http://www.jbc.org/>. print.  
ISSN: 0021-9258.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
AB Antigen three-dimensional structure potentially limits antigen processing and presentation to helper T-cell epitopes. The association of helper T-cell epitopes with the mobile loop in Hsp10s from mycobacteria and bacteriophage T4 suggests that the mobile loop facilitates proteolytic processing and presentation of adjacent sequences. Sites of initial proteolytic cleavage were mapped in divergent Hsp10s after treatment with a variety of proteases including cathepsin S. Each protease preferentially cleaved the Hsp10s in the mobile loop. Flexibility in the 22-residue mobile loop most probably allows it to conform to protease active sites. Three variants of the bacteriophage T4 Hsp10 were constructed with deletions in the mobile loop to test the hypothesis that shorter loops would be less sensitive to proteolysis. The two largest deletions effectively inhibited proteolysis by several proteases. Circular dichroism spectra and chemical cross-linking of the deletion variants indicate that the secondary and quaternary structures of the variants are native-like, and all three variants were more thermostable than the wild-type Hsp10. Local structural flexibility appears to be a general requirement for proteolytic sensitivity, and thus, it could be an important factor in antigen processing and helper T-cell epitope immunogenicity.

L20 ANSWER 18 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:186871 BIOSIS  
DOCUMENT NUMBER: PREV200100186871  
TITLE: The git5 Gbeta and git11 Ggamma form an atypical Gbetagamma dimer acting in the fission yeast glucose/cAMP pathway.  
AUTHOR(S): Landry, Sheila; Hoffman, Charles S. (1)  
CORPORATE SOURCE: (1) Biology Department, Boston College, Higgins Hall 401B, Chestnut Hill, MA, 02467; hoffmacs@bc.edu USA  
SOURCE: Genetics, (March, 2001) Vol. 157, No. 3, pp. 1159-1168. print.  
ISSN: 0016-6731.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Fission yeast adenylate cyclase, like mammalian adenylate cyclases, is regulated by a heterotrimeric G protein. The gpa2 Galpha and git5 Gbeta are both required for glucose-triggered cAMP signaling. The git5 Gbeta is a unique member of the Gbeta family in that it lacks an amino-terminal coiled-coil domain shown to be essential for mammalian Gbeta folding and interaction with Ggamma subunits. Using a git5 bait in a two-hybrid screen, we identified the git11 Ggamma gene. Co-immunoprecipitation studies confirm the composition of this Gbetagamma dimer. Cells deleted for git11 are defective in glucose repression of both fbp1 transcription and sexual development, resembling cells lacking either the gpa2 Galpha or the git5 Gbeta. Overexpression of the gpa2 Galpha partially suppresses loss of either the git5 Gbeta or the git11 Ggamma, while mutational activation of the Galpha fully suppresses loss of either Gbeta or Ggamma. Deletion of gpa2 (Galpha), git5 (Gbeta), or git11 (Ggamma) confer quantitatively distinct effects on fbp1 repression, indicating that the gpa2 Galpha subunit remains partially active in the absence of the Gbetagamma dimer and that the git5 Gbeta subunit remains partially active in the absence of the git11 Ggamma.

subunit. The addition of the CAAX box from the git11 Ggamma to the carboxy-terminus of the git5 Gbeta partially suppresses the loss of the Ggamma. Thus the Ggamma in this system is presumably required for localization of the Gbetagamma dimer but not for folding of the Gbeta subunit. In mammalian cells, the essential roles of the Gbeta amino-terminal coiled-coil domains and Ggamma partners in Gbeta folding may therefore reflect a mechanism used by cells that express multiple forms of both Gbeta and Ggamma subunits to regulate the composition and activity of its G proteins.

L20 ANSWER 19 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:215512 BIOSIS  
DOCUMENT NUMBER: PREV200000215512  
TITLE: Helper T-cell epitope immunodominance associated with structurally stable segments of hen egg lysozyme and HIV gp120.  
AUTHOR(S): Landry, Samuel J. (1)  
CORPORATE SOURCE: (1) Department of Biochemistry, Tulane University School of Medicine, 1430 Tulane Avenue, New Orleans, LA, 70112 USA  
SOURCE: Journal of Theoretical Biology, (April 7, 2000) Vol. 203, No. 3, pp. 189-201.  
ISSN: 0022-5193.

DOCUMENT TYPE: Article  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Although many antigen sequences potentially can bind to the MHCII proteins, only a small number of epitopes dominate the immune response. Additional mechanisms of processing, presentation or recognition must restrict the immune response against a large portion of the antigen. A highly significant correlation is found between epitope immunodominance and local structural stability in hen egg lysozyme. Since antigen proteins are likely to retain substantial native-like structure in the processing compartment, protease action may be focused on regions that are most readily accommodated in the protease active sites, and thus, the intervening sequence are preferentially presented. Immunodominance also correlates with sequence conservation as expected from the constraints imposed by structure. These results suggest that the three-dimensional structure of the antigen limits the immune response against some antigen segments. For HIV gp120, a substantial improvement in the accuracy of epitope prediction is obtained by combining rules for MHCII binding with a restriction of the predicted epitopes to well-conserved sequences.

L20 ANSWER 20 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1998:33648 BIOSIS  
DOCUMENT NUMBER: PREV199800033648  
TITLE: Local protein instability predictive of helper T-cell epitopes.  
AUTHOR(S): Landry, Samuel J. (1)  
CORPORATE SOURCE: (1) Dep. Biochem., Tulane Univ. Sch. Med., 1430 Tulane Ave., New Orleans, LA 70112 USA  
SOURCE: Immunology Today, (Nov., 1997) Vol. 18, No. 11, pp. 527-532.  
ISSN: 0167-5699.

DOCUMENT TYPE: Article  
LANGUAGE: English

L20 ANSWER 21 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1996:310456 BIOSIS  
DOCUMENT NUMBER: PREV199699032812  
TITLE: Expression and purification of I-kappa-B-alpha protein.  
AUTHOR(S): Liang, Li (1); Steede, N. K.; Landry, S. J.  
CORPORATE SOURCE: (1) Dep. Chem., Xavier Univ., New Orleans, LA 70002 USA  
SOURCE: FASEB Journal, (1996) Vol. 10, No. 6, pp. A1519.  
Meeting Info.: Joint Meeting of the American Society for Biochemistry and Molecular Biology, the American Society for Investigative Pathology and the American Association of Immunologists New Orleans, Louisiana, USA June 2-6, 1996  
ISSN: 0892-6638.  
DOCUMENT TYPE: Conference  
LANGUAGE: English